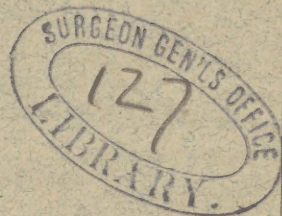


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WITH REMARKS.



BY  
GEORGE ROSS, A.M., M.D.,

Professor Clinical Medicine, McGill University, Attending Physician Montreal General Hospital. Reported by Mr. H. N. Vineberg, Clinical Clerk.

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## TYPICAL CASE OF ADDISON'S DISEASE.

WITH REMARKS.

BY GEORGE ROSS, A.M., M.D.

Professor of Clinical Medicine, McGill University, Attending Physician Montreal General Hospital. Reported by Mr. H. N. Vineberg, Clinical Clerk.

J. F., æt. 23, coal carter, was admitted into the Montreal General Hospital, on the 9th June, 1877, under the care of Dr. Ross, suffering from discolouration of the skin, pain in the stomach, vomiting and weakness.

Nothing can be learned concerning his previous family history except that his father and mother are both living, and no account of tuberculous disorders can be heard of amongst any other members of the family.

He himself it seems took very early to drinking habitually, getting very drunk quite frequently. He was, in consequence, necessarily exposed to much hardship, sometimes even lying out in the cold and rain. He continued thus intemperate until about two years ago, when his present ill-health began. Up to this time he says he never knew what it was to be sick. He then began to complain of being weak, and suffered from giddiness a good deal, and sometimes from pain in the front part of the head. He continued, however, to work until last fall, but often feeling that he was not strong enough for it. The giddiness also kept increasing, so much so that he many times when stooping down, rolled over quite helpless, and he was often suspected of being drunk. Is not aware of having ever strained himself, but, of course, did very labourious work. His appetite had been failing and he was becoming very singular in his selection of food. For instance, he could not eat butter, but insisted upon having *lard*, and he had a strong craving for *acids*, especially pickles and vinegar, which latter (if his father can be believed) he would drink pure by the pint at a time. He also had attacks of *vomiting* not unfrequently, even whilst at work, and often suffered from pains in various parts of the body—"all over him" as he says. Besides these, the following symptoms have also been observed, and have been growing steadily more marked since last winter. *Breathlessness* upon the least exertion. *Drowsiness*, tending at once to fall asleep if left to himself, and such intense *feebleness* that he could not possibly



walk straight. The latter being most marked immediately after getting up in the morning, when he reels and staggers about like a drunken man. Cold *extremities*, especially his hands: his father remarked him wearing mits in warm weather, and often going to the stove to warm his feet. It is somewhat more than a year since the *discolouration* of the skin was first noticed by his friends, but it certainly existed much longer, because it was learnt that last summer his father, on coming home after an absence of just a year, hardly recognized his own son, owing to the great change which had meantime occurred in the colour of his skin. He has never fainted, and is not aware of having had attacks of palpitation of the heart.

*Present Condition.* Patient is a man rather above the ordinary size, well-built and well-nourished. He has brown hair and brown eyes. He lies in bed with a dull, heavy and stupid expression, and when left alone is continually sleeping; in fact, it is difficult to keep him awake long enough to get from him answers to a question or two, and even then means have to be taken to keep up his attention or he would immediately relapse into the same lethargic slumber. When first roused up he whines and laments like a child, making piteous kind of grimaces, the forehead contracted and the angles of the mouth drawn up. Having gone through this performance, it is generally necessary to repeat a question two or three times before any intelligible answer can be procured. The entire skin of his body is of a dark brown colour, resembling in appearance that of a Malay or a white man who had been deeply stained with walnut juice. It in all respects agrees perfectly with the descriptions given of the most typical cases of *Morbus Addisonii*—The discolouration is most deep upon the face, neck, nipples, lower part of the abdomen, penis and scrotum, and the backs of the hands. It is least marked over the lower extremities. The pigment is particularly intense on the genital organs, which indeed are nearly as dark as in a veritable negro. The backs of the hands are of an extremely dark mahogany brown, the colour terminating by an abrupt margin on the lateral aspects and contrasting strongly with the corresponding palms which are comparatively quite pale. The line of boundary of the pale portion in the palm is also well seen on the anterior aspects of the wrists at which part the deep colour of the forearm suddenly ends by an abrupt straight margin. There are several very dark brown (almost black) circular spots or moles upon both cheeks,

and a few also upon the front of the abdomen and upon the back. The *mucous membrane* of the lips, cheeks and tongue, all show marked black pigmentary mottlings and patches. The inside of the lower lip presents about its middle a beautiful generally distributed marbled appearance. At the inner margin of the red exposed portion of the lower lip is to be seen an irregularly scalloped dark line, about one line in width and running the whole length of the lip. There is also a black patch on the gum of the lower jaw at a spot corresponding with the two left incisor teeth. On the left side of the tongue are two similar dark blotches, one near the tip and the other a little further back, these look just as though the back of a pen had been rubbed over them.

All the mucous membranes visible are of a healthy red colour, the nails of the fingers and toes are also of the ordinary pink colour of health. The eyes are somewhat bloodshot, pupils moderately contracted and respond freely to light, Temperature 100.2° F. Tongue rather coated with a light brownish fur. Appetite bad. Bowels rather loose. Pulse, 80, small, weak and very easily compressed. Heart sounds distinct but markedly feeble; not accompanied by any murmurs. Apex beat in normal situation. Lungs healthy, Liver and spleen occupying their proper areas. No abdominal pulsation detected. Has passed no urine since admission yesterday: withdrew 6 oz. with catheter. It is high coloured, sp. gr. 1008, no albumen, no sugar, becomes very dark when boiled with nitric acid.

There seems to be some general hyperæsthesia, as a moderate squeeze anywhere will cause him at once to whine and cry out. Complains much of pains everywhere, and especially headache. He was got out of bed and ordered to walk across the ward, when he plunged and staggered along in the most headlong way and would have fallen at once if not supported. He begged to be allowed back to bed, and threw himself down utterly exhausted and his heart beating very rapidly.

Blood from the finger was examined; no increase in the number of the white blood corpuscles. The fibrine fibrils were unusually distinct, otherwise it was quite natural. Schultz's "granular masses," so common in cachectic states, were not observed.

*Ordered.* Milk diet with beef tea and  $\mathcal{R}$ . Morph. sulphat gr.  $\frac{7}{6}$   
Bism. nitrat. gr. x. every six hours.

11th June. Passed a very restless night, whines and cries to-



day even more than yesterday. Vomited several times during the night and morning. Takes no food, but craves water continually, but when given to him often does not drink any. Severe headache, very weak and staggering when trying to stand. Passed a considerable amount of urine, sp. gr. 1010. No albumen. Temperature,  $98.4^{\circ}$  F.

*12th June.* Somewhat quieter and more rational to-day; takes more nourishment, but vomited two or three times through the night, and now sitting up at once brings on an inclination to vomit. His eyes were examined to-day by Dr. Buller; no abnormal appearances were noticed. The pigment in the fundus was abundant, but not unusually so for a dark-haired person.

*13th June.* Had a bad night and seems worse to-day, very weak and complains much. Is somewhat deaf. No vomiting since yesterday. Passed a very copious stool yesterday of a singular grey colour. Pulse remains small, weak and compressible, 80 per minute. Temp.  $96.4^{\circ}$  F. Other symptoms unaltered.

Ordered 3 oz. wine daily.

*14th June.* A much better night. Seems singularly improved to-day; makes no complaint of pain of his own accord, but when asked says he has pain in his back and down his legs. Had three motions similar to that described. No vomiting. Tongue moist, and only very slightly coated. Pulse rather better, not so shabby as during last three days. Temperature,  $95.4^{\circ}$  F. and  $97.8^{\circ}$  F. Blood again examined, same result, exactly, as before.

*15th June.* Slept well last night; seems better than any day yet; does not whine and complain at all; is much more intelligent, and answers questions quite readily; not nearly so drowsy as he has been; is taking food well; cannot stand upright without being supported. Urine as before. Temperature,  $95.4^{\circ}$  F. and  $97.8^{\circ}$  F.

*16th June.* About as yesterday, still pains in back and down the legs. Temperature,  $95.4^{\circ}$  F. and  $96.4^{\circ}$  F.

*17th June.* Not so well to-day; pains all over; sleeps nearly all the time. Pulse about 90, but very difficult to count, it is so extremely small and shabby. The foregoing note was made at 11 a.m., and he continued about the same way until 7 p.m., when he became very restless, crying out to send for his father. He was now seen by one of the resident physicians, who found him rolling about in bed, covered with a cold clammy sweat. Pulse very small and irregular, and complaining of general pains and especially cramps in the left leg. Frictions and warmth, together with



stimulants, internal and external, were freely used, but with only temporary rallying effect, for within three-quarters of an hour he was evidently moribund, and died at 8.15 p.m.

AUTOPSY, BY DR. OSLER, 16 HOURS P. M.

Body that of a tall, well-formed young man. Muscles of average development, and in good condition. Panniculus adiposus scanty. Skin presents the appearance described in the clinical report. Rigor mortis present.

*Thorax*.—Muscles of a healthy red colour. *Thymus gland* appears enlarged, weighs  $\frac{3}{4}$  vi. On examination only the normal elements are found.

*Heart*, 240 grms. Right auricle distended with blood, and on opening it 3 to 4 ounces of dark semi-coagulated blood escaped. Right ventricle also full of grumous clots. Left auricle contains blood; Left ventricle contracted and empty. On removal of the organ fully 14 oz. of blood escaped. Valves and orifices healthy. Muscular substance of good colour; the fibres are slightly granular, but the striæ are not obscured, and there are no definite oil droplets to be seen. *Aorta*, healthy.

*Lungs*, crepitant throughout; no adhesions; no nodules, tubercles, or caseous masses.

*Abdomen*. Viscera look natural.

*Spleen* not enlarged, slightly adherent to the diaphragm. Consistence good. Malpighian corpuscles distinct. Structure normal.

*Kidneys*.—Capsules detach easily, surfaces smooth; one or two small cysts noticed. On section Malpighian corpuscles prominent, cortices and medullæ, with the exception of the mammillæ, of a dark brownish-red colour. Nothing abnormal found on microscopical examination.

*Supra-renal Capsules*.—Left feels firm, and is bound to the neighbouring parts by fibrous adhesions which were with difficulty torn through. On removal it weighs 3 vss., and has lost its cocked hat shape, being somewhat oval, and about the size of a large testicle. The surface is irregular, puckered, and here and there round nodules softer than the rest project. Two thin remnants of the gland are attached to the central mass. One, an inch in length, passed downwards from the posterior part, and in it are several small caseous nodules; the other, springing from the anterior part, is not so marked, and contains no nodules. One good-sized artery and two small ones enter the gland at the lower border. A few nerves of ordinary appearance are seen going to it.

On section with a sharp knife, it cuts with considerable resistance, and is seen to be made up of central caseous masses, surrounded by dense semi-translucent fibrous tissue, 3''' to 4''' in thickness, and in places very firm and hard. The caseous masses are separated indistinctly into two portions by a strand of gelatinous-looking tissue, and are firm, greyish-yellow or cream coloured, soft at the periphery so that they can readily be peeled out of the fibrous investments. In one central spot the caseous matter is becoming very dry and cretaceous. *The right capsule* is larger than the left, and lies in its normal position on top of the kidney and in contact with the liver, to which it is united by fibrous bands. The investing fat is in small amount, but very fibrous. The organ has completely lost its flattened shape, and appears made up of two irregular nodules, the upper of which projects towards the liver, the lower, somewhat triangular in shape, passing down towards the hilum of the kidney, and to its under surface the renal vein is attached. To the touch they are firm and elastic. Two medium-sized arteries, one a branch of the renal, enter at the lower border. A few nervous cords are seen entering the gland, but they are neither numerous nor large. On section essentially the same condition is found as in the other organ; the upper mass has a firm caseous centre, of a uniform greyish-yellow colour, moist, not friable, and softening only at the margins where it is in contact with the fibrous capsules. In the other portion the caseous matter is softer, here and there cretaceous, and interspersed with gelatinous looking fibrous tissue.

On examination the central caseous masses present nothing of interest, being composed of a finely granular debris in which the remains of degenerated cells and fibres may be seen.

Scrapings from the inner surface of the fibrous capsules show a large number of small lymphoid corpuscles, finely granular, and not very distinctly nucleated. A few are large and more granular. With these are numerous spindle-shaped fibre cells, which are the chief elements in the investing capsules, the lymphoid corpuscles occurring in groups or scattered irregularly among them. In the soft gelatinous-looking tissue immediately surrounding the caseous masses and often penetrating them, in addition to the above elements, which also occur in variable numbers, there are found:—

(1) Cells two or three times the size of white blood corpuscles, with one or two nuclei. Many are in a condition of fatty degenera-



tion, others have been converted into the compound granule corpuscles.

(2) Numerous corpuscles resembling the nerve cells described as occurring in the adrenals. They are chiefly unipolar, with coarsely granular protoplasm and single nuclei, and with a long process passing off from the body of the cells, rendering them club-shaped; corpuscles with two or three processes are also common. Many of these look very like ganglion cells, in others the processes are more irregular and the resemblance is less striking.

(3) Giant cells, of which a number of well marked specimens were found.

*Bladder* contains about  $\frac{2}{3}$  x of clear normal urine. Walls healthy.

*Stomach.* Large veins full, small vessels of mucous membrane at the fundus also injected; rest of the membrane pale. Scattered throughout the whole mucosa, but chiefly about the cardiac and pyloric extremities, are numerous small, round, white bodies, looking like little lenticular glands. Some of them present small orifices in communication with the surface, as if they had ruptured or ulcerated at these points. On examination they are found to be localized lymphoid infiltrations of the mucosa.

*Duodenum* is blood-stained, and the small vessels are full of blood.

*Jejunum*, and *Ileum* contain a small amount of dark tarry fæces, loosely adherent to the mucous membrane. The large veins are injected. The solitary glands and patches of Peyer are slightly enlarged. Here and there on the mucous membrane of the jejunum are small dark spots which cannot be washed off and appear to be pigmentary depositions. About six or eight feet from the ilco-cæcal valve a portion of the intestine 8" in length is curiously thickened, being at least five times as thick as the adjacent parts, and of a somewhat brownish-yellow color. Several thick, partially developed, valvulæ conniventes are seen on the mucous surface. On section the surface is uniform, presenting no separation of mucous and muscular coats.

*Large intestine* presents nothing abnormal. The solitary glands are very distinct in the cæcum. There are several masses of dark fæces in the descending colon.

*Liver.* Weight, grms. 900. Capsule slightly thickened, especially over the gall bladder. On section, organ looks healthy, surface is uniformly reddened, acini not very distinct. The veins contain

a good deal of blood. In certain regions the substance beneath the capsule is stained of a dark colour; on examination this is found to be due to an accumulation of dark pigment grains in the liver cells, which were, as a rule, slightly granular, and here and there contained oil drops.

The *lymphatic glands* of the abdomen, including those of the mesentery, were a little enlarged; one or two were removed with the supra-renal capsules.

The celiac axis with *semilunar ganglion* and attached nerves were carefully removed. Nothing unusual was observed about them, the sheaths of the nerves were not thickened, and the cells presented a natural appearance. Long splanchnic nerves and dorsal and lumbar ganglia of the sympathetic also examined. All these parts were compared with those of a woman, aged 40, dead of heart disease, on whom an autopsy was made on the same day, and no appreciable differences found.<sup>1</sup>

*Marrow* of ribs of a light red colour, abundant, and evidently fatty. On examination, red blood corpuscles exceed all other elements. Marrow cells of usual appearance. The small lymphoid corpuscles, so often met with in marrow, were not noticed. Fat globules more numerous than usual in the ribs. No nucleated red corpuscles, myeloplques, or corpuscles containing red blood cells noticed.

*Remarks.* I believe this to be the first genuine case of uncomplicated Addison's Disease which has been publicly communicated or published in Canada. The only other report of which I am aware is one by Prof. MacCallum of Montreal, published in the *Medical Chronicle* for the year 1857. This case, however, must, I am inclined to think, be looked upon as somewhat doubtful. The patient was the subject of ordinary pulmonary phthisis, and when first seen was in an advanced condition of emaciation, with, at the same time, all the ordinary symptoms and physical signs of this disease. He was distinctly bronzed on the face, back

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1 It is only just to state, with reference to the condition of the nerves going to the capsules, that no dissection of them was made *in situ* for the following reason: On the evening of the patient's death the father positively refused, in spite of all arguments, to allow of an autopsy, and, as he was going to remove the body in the morning, the supra-renal capsules, with the kidneys and portions of the liver and spleen, were taken out that night *per vias an naturales*, viz., through the rectum. It was done without any tearing of the capsules, and the right one was removed attached to the kidney. On the following day the father was in a better state of mind, and consented to an examination, when, as above mentioned, the celiac axis, with the semi-lunar ganglion and attached nerves were removed.



and hands and in the axillæ. On the chest he had a patchy discolouration which was probably chloasma. Affection of the supra-renal capsules was suspected by Dr. MacCallum during life and after death one of these was found much enlarged, tough and almost cartilaginous; the other was soft, easily broken down and showed no sign of disease. Thus here the only relation with Addison's Disease was the discolouration (which is well known to be *alone* entirely fallacious as a sign) and pathologically there was found none of the true caseous disease in any of its forms, which alone constitutes the invariable morbid lesion of this disease, according to Wilks, Greenhow and other recent observers.

The case just read may be looked upon as a typical and uncomplicated case of Addison's Disease. As far as the clinical features of this affection are concerned, they have now been studied by a great many observers, and the essentials may be considered as pretty clearly settled. It is interesting to observe how little in this way has been done to add to the original delineation of the complaint given by Addison himself. But a great deal has undoubtedly been done to elucidate its pathology and to establish the certainty of the morbid lesion—which had long been doubtful, and even yet is not universally admitted. The names of Drs. Greenhow, Wilks, and Habershon are those which are most prominent in this connection. I would like to make a few remarks upon certain of the prominent symptoms which have been above detailed, and on the bearing of some of the facts upon certain doctrines newly broached concerning the alliance between this disease and some forms of anæmia, especially progressive pernicious anæmia.

*The Asthenia.* To show to what a remarkable degree this profound debility was present, I need only recall some of the symptoms to which it naturally gave rise, the inability to stand, the great languor and indisposition for the least exertion, the incapability to grasp with any degree of power, and all this without any apparent diminution in the bulk of the muscles, or any sufficient degree of emaciation. In many descriptions of this disease *anæmia* is placed along with *asthenia* and often made to some extent to account for the latter; but I think it may very well be doubted if anæmia be really an *essential* part of the affection. Certainly this case tends rather to support the idea that the most profound degrees of asthenia and prostration may be induced by supra-renal disease, without being accompanied by any

of those changes in the blood going under the common term *anæmia*. It will be observed that the report states that there were none of the ordinary rational signs of *anæmia* present; the mucous membranes, where visible, were as red as in health, the nails were quite pink, not white, there was no cardiac bruit, the blood, when drawn, was not at all watery-looking, and microscopical examination of the same proved that its cellular elements appeared just as in health. At the autopsy the muscles were found containing abundance of blood, of good consistence, and of the usual full bright red colour of perfect health. It is plain that it needs but one such case properly substantiated to show that the fully developed affection may exist and may prove fatal without there having, at any time, been the least appreciable *anæmia*. This is an interesting point to settle. Dr. Addison, in his original description, placed *anæmia* *first* amongst the prominent symptoms present; and quite lately Prof. Pepper, of Philadelphia, has, in an able paper, tried to substantiate an alliance between Addison's Disease and some forms of chronic wasting disease, all accompanied by profound *anæmia* and which he proposes to call *Anæmotosis*. There is no denying the fact that it is quite common to find patients with this disease decidedly *anæmic*, but that might naturally be expected as a secondary result, from impaired digestion and nutrition. It would be impossible within the limits of these remarks to endeavour to contravert the views of Prof. Pepper, but I must content myself with drawing attention to the entirely negative results of this typical case, as wholly opposed to his theory. This is simply in accordance with the experience of Dr. Greenhow, for he says "so far as I have been able to ascertain, the composition of the blood does not undergo any important alteration in uncomplicated cases of Addison's Disease." I have also under observation at the present time (singularly enough, considering the rarity of the complaint) a second patient, a female, with intense bronze skin, and who, I am convinced, is the subject of supra-renal disease. Her symptoms are, though not so intense, yet just as characteristic of the *Morbus Addisonii* as were those in the case of J. F. just read. She has been for ten days at a time in my wards of the Hospital and has been thoroughly examined. Now this woman, also, though very weak and listless, and suffering from frequent palpitation, yet shows no signs of *anæmia*; her mucous membranes and nails look quite bright and red, there is no cardiac bruit, and, under the microscope, the blood appears per-



fectly natural. I might mention that in these microscopical examinations I have had the valuable assistance of my colleague Dr. Osler, and therefore, from his known skill and experience in this department, complete reliance can be placed upon the results obtained in both these cases. Thus I am convinced that, though anæmia is very common in Addison's Disease, yet that the essential pathology of this affection is not to be looked for in the blood. Prof. Pepper, in regarding this disease as of *hæmic* origin, has suggested that probably the marrow is at fault, as it certainly is in some of the special forms of anæmia. But, in our case, the marrow of all the long bones was submitted to careful microscopical examination and found presenting nothing but the usual healthy appearances.

*Pains* in various parts were much complained of. The principal site of these was across the abdomen, in the back, and down the thighs. In the female patient to whom I have just alluded similar pains have been felt for several months. For a long time, on one occasion, it occupied the region of the left sciatic nerve, and she was treated for sciatica.

*Vomiting* occurred very frequently, generally spontaneously, in an explosive sort of way, but sometimes came on as soon as he was made to sit up or to turn round in bed.

*The physiognomy and mental condition* were both very peculiar. The odd way in which he would whinge and half-cry when spoken to has been alluded to, as well as the puerility of his whole conduct. This state was to me very singular. I am not aware of having noticed anything exactly like it in any other disease. I do not find that this is specially noted in many of the collected cases of Dr. Greenhow, but the very first case of Addison's collection describes it exactly. He says: "the voice is puny and puerile, the patient speaking with a kind of indescribable whine, and his whole demeanor is childish." I would also remark here the way in which these symptoms abated to a great extent for a few days before his death. This was co-incident with improvement in almost all the symptoms. This tendency to *intermissions*, even in advanced cases of this disease, has often been noticed.

*The temperature* followed the general rule, of being almost constantly subnormal, although before his admission there was slight elevation of temperature, probably to be accounted for by some local inflammatory action.

As regards the *date of appearance* of the *discolouration*, in connection with the general symptoms, it was impossible to establish

it very definitely. He was a coal carter, and consequently it would take a considerable degree of darkening to be appreciable through his normally smutty skin. But, as stated, I think from what we could learn, that he was ailing several months before discolouration began, which also would be in accordance with what has usually been observed.

*His occupation* calls for a word. He was a coal carter, and therefore much exposed to very heavy manual labor, and frequent heavy lifts and strains. According to Greenhow, the great majority of all cases occur in the lower and the hard-working classes; and he is inclined to attribute some importance to the fact, because he thinks that the disease may, perhaps, be often originated by some violent wrench or strain upon the loins.

*The supra renal capsules* were in a stage very commonly met with, viz., that of extensive caseous deposit, with some softening—a sort of medium stage, not having advanced either to the completely-softened or puriform stage, nor to the still later cretiform stage, which is sometimes seen, with shrinking of the organ. They were surrounded by very dense and firm connective tissue. The exact connections of this, and the manner in which it involved the surrounding nerves, could not, I regret to say, be as carefully examined as I could have wished, owing, as already explained, to the somewhat peculiar manner in which the autopsy was originally performed. The view adopted by Dr. Greenhow, and very generally accepted, that the disease is caused in some way or other by involvement of large branches of the sympathetic and other nerves in an advancing sclerosis of the adjacent areolar tissue has, I think, everything to commend it. It is certainly the only theory yet given capable of at all explaining the peculiarities of this truly singular disease. One grave argument against it is that a great many cases have been recorded where no lesion of these nerves could be detected: this case adds one more to the number of these, for, though the branches going to the glands were carefully examined, nothing abnormal could be found.











